

## **REMARKS**

### **The Amendments**

The claims are amended to conform to the claims that were allowed in granted EP Patent No. 1,457,208 B9. By this amendment, part of the substance of claims 2 and 20 is incorporated into claim 1; see, e.g., also page 8, lines 30-34, of the specification, supporting the amendment. Withdrawn claims 7-19 and 26-28 are canceled. New dependent composition and method claims are added. Support for the new claims is found in the original disclosure as a whole, for example, see: page 10, lines 1-7; page 9, lines 9-10; page 15, lines 6-9; page 1, lines 8-10; page 1, lines 15-33; page 4, lines 28-35; page 23, lines 19-30; page 14, lines 22-34; and page 8, lines 36-37.

Applicants reserve the right to file one or more continuing and/or divisional applications directed to any subject matter disclosed in the application which has been canceled by any of the above amendments.

### **The Restriction Requirement**

The claims non-elected pursuant to the restriction requirement are canceled. However, new method of use claims dependent on the composition claims have been added. If a similar ground of restriction is made against these new claims, applicants will maintain their traversal of the restriction for the same reasons. A method which is conducted with a materially different product will not result in the same method. A materially different product has different properties. Thus, practicing the method with a materially different product will result in a

materially different method, not the same method. As a result, the factual basis for the restriction is not supported and the restriction should be withdrawn. Applicants also urge that, should the composition claims be found allowable, the method claims will be subject to rejoinder.

Reference is made to the decisions in In re Ochiai, 37 USPQ2d 1127 (Fed. Cir. 1995), and In re Brouwer, 37 USPQ2d 1663 (Fed. Cir. 1996). The Commissioner's comments thereon in 1184 TMOG 86, March 26, 1996, indicate that where product and process claims in the same application have been restricted and the elected product claim has been found allowable, withdrawn process claims including the limitations of the allowed product claim will be rejoined into the application and fully examined in that same application. If the restriction is not withdrawn, the method of use process claims herein should be rejoined and fully examined at such time as the product claim is found allowable.

### **The Rejection under 35 U.S.C. §103**

The rejection of claims 1-6 and 20-25 under 35 U.S.C. §103, as being obvious over WO 95/12383 in view of Riffkin (J.Pharm.Sc.), is respectfully traversed.

As stated in the Office action, WO '383 discloses an injectable solution of testosterone undecanoate with an injectable plant oil and/or benzyl benzoate. As also noted in the Office action, WO '383 provides no suggestion to use castor oil as the plant oil in its compositions. To the contrary, at page 4 of the publication, WO '383 recites the possible use of peanut, soy, sesame, tea or olive oils. WO '383 also provides no suggestion as to the relative amounts of the plant oil and benzyl benzoate. Particularly, there is no suggestion of a composition containing an amount of castor oil as recited in the current claims, i.e., castor oil in a concentration of 25 to

45% by volume.

The Office action alleges that it would have been obvious to one of ordinary skill in the art to modify the teachings of WO '383 in view of Riffkin since Riffkin teaches the use of a vehicle having castor oil and benzyl benzoate in relative amounts of 1:1 (50:50) or 65:35 for delivering steroidal compositions parenterally. Riffkin discusses the use a combination of castor oil and benzyl benzoate as a vehicle for steroid hormones generally. However, Riffkin discloses no such combination of a vehicles with a testosterone ester. Riffkin discloses 9 examples of vehicles with castor oil and benzyl benzoate. In these vehicles the amount of castor oil ranges from 50 to 80%.

Applicants respectfully submit that one of ordinary skill in the art would not have been motivated or otherwise had a reason to modify the compositions of WO '383 to provide a composition meeting the requirements of the instant claims. If one of ordinary skill in the art were to modify the WO '383 compositions in view of Riffkin, they would use castor oil as the plant oil in an amount of 50-80% in the composition according to Riffkin's teachings. Such a composition would not meet the recitations of the instant claims, i.e., a vehicle comprising castor oil in a concentration of 25 to 45% by volume. There are no other suggestions from the cited references to provide a composition, as claimed, having this amount of castor oil. For this reason alone, it is urged that the cited references fail to establish a prima facie case for obviousness and the rejection under 35 U.S.C. §103 is not supported.

Additionally, the cited prior art fails to teach or suggest the advantages for the claimed compositions discovered by applicants. Applicants' specification states (page 10, lines 24-33):

The compositions of the invention are chemically stable with respect to the

testosterone esters. That is to say that degradation products could not be detected after long term storage (such as after 7 weeks or 17 weeks or even longer) at conditions normally known to accelerate degradation processes, such as variations in temperatures, high and low temperatures and various relative humidity. For example, less than 1% by weight of degradation products of testosterone esters is present after storage of the composition for at least 7 weeks, such as for 16 or 17 weeks, for 6 months, or for 9 or 12 months at 40 °C and 25 % RH in darkness. Preferably, less than 0.5 % w/w, such as less than 0.2 % w/w of degradation products of testosterone esters is present after storage at the above-mentioned conditions.

The references do not teach or suggest the advantageous stability properties.

As further proof of this advantage of applicants' invention and as further proof of the nonobviousness of the claimed invention, applicants submit herewith a Declaration under 37 C.F.R. §1.132 showing the unexpected advantages of applicants' invention. The declaration provides side-by-side comparisons of the stability of compositions according to the claimed invention with compositions otherwise the same but having higher amounts of castor oil, such as taught by Riffkin. Multiple ampoules of compositions containing testosterone undecanoate, benzyl benzoate and castor oil were tested side-by-side for stability (lack of precipitate crystals) over 34 days. One set of ampoules contained 60% castor oil, one set 50% and one set 37%. All of the ampoules which contained 37% castor oil (63% benzyl benzoate) – and thus are representative of the claimed invention – maintained stability with no precipitate for the full 34 days. For the compositions which contained 50% – the lowest range suggested by Riffkin – and 60% castor oil, most of the ampoules lost stability before 34 days.

The advantage in stability of the compositions, when using a lower amount of castor oil as recited in the instant claims, could not have been expected from the prior art. Neither reference teaches any advantage in stability for its compositions. Further, to the extent Riffkin

suggests to use castor oil in the WO '383 compositions, it only suggests to use such in amounts of 50% or higher. Thus, the advantage in stability of the solutions for applicants' invention using a lower amount of castor oil was clearly unexpected over the prior art teachings. This unexpected advantage provides further clear and convincing proof of the nonobviousness of applicants' invention.

The declaration also provides comparisons of castor oil to peanut oil and miglyol solutions. These comparisons clearly show that castor oil is advantageous to these other oils. Thus, the comparison also shows the advantage in stability of the solutions of the claimed invention using castor oil over those having the first-listed preferred oil of WO '383, i.e., peanut oil. Again, since the references suggest no advantage in stability, this data further evidences the advantages of applicants' invention are unexpected and further support nonobviousness.

For all of the above reasons, it is urged that the combined teachings of WO '383 in view of Riffkin, and considered in light of the declaration evidence of nonobviousness, fail to render the claimed invention obvious to one of ordinary skill in the art. Thus, the rejection under 35 U.S.C. §103 should be withdrawn.

It is submitted that the claims are in condition for allowance. However, the Examiner is kindly invited to contact the undersigned to discuss any unresolved matters.

The Commissioner is hereby authorized to charge any fees associated with this response or credit any overpayment to Deposit Account No. 13-3402.

Respectfully submitted,

/John A. Sopp/

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